Comments from the Environmental Working Group

Proposed Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act

Docket ID: EPA-HQ-OPPT-2016-0654-0001

March 20, 2017

Introduction

The Environmental Working Group (EWG) is a nonprofit advocacy organization dedicated to improving environmental health. EWG has spent over a decade advocating for reforms to strengthen the Toxic Substances Control Act (TSCA). The Frank R. Lautenberg Chemical Safety for the 21st Century Act (hereinafter "Lautenberg Act") for the first time requires the Environmental Protection Agency (EPA) to comprehensively review existing chemicals on the TSCA inventory.

EPA's risk evaluation procedure rule will delineate the process by which EPA evaluates chemicals to determine which are in need of restrictions to protect human health and the environment. This is a critical part of implementing the new requirements under the Lautenberg Act. It is imperative that EPA craft a transparent procedural rule that rigorously evaluates chemical safety based on adequate information about hazards and exposures, accounts for vulnerable subpopulations, and provides sufficient flexibility to account for varied conditions of use and changes in scientific understanding. EWG appreciates the opportunity to weigh in and specifically comments that:

- EPA should not codify definitions of scientific standards like "best available science."
- EPA should not codify the definition of unreasonable risk and should modify the factors listed in the preamble.
- EWG supports the proposed expanded definition for potentially exposed and susceptible subpopulations.
- Manufacturer-requested chemical reviews must be based on adequate information, account for potential biases, and undergo the same rigorous review as prioritized chemicals.

- When defining the scope of a risk assessment, EPA should actively seek out information about all conditions of use throughout the lifecycle of the substance, as well as the real-world exposures of vulnerable and chemically overburdened populations.
- EPA should use systematic review procedures to evaluate chemicals, but should not define systematic review, or weight of evidence, in the rule.
- EPA should use aggregate and cumulative exposure analysis whenever possible, and should limit use of sentinel exposure evaluation.
- EPA should use population-based risk assessments instead of using margin of exposure analysis for non-cancer endpoints.
- EPA should issue guidance on draft risk assessments by interested persons who require such assessments, at a minimum, to meet the same requirements as those in the finalized risk evaluation rule.

No part of these comments should be construed as requiring EPA to reissue a proposed rule. EWG is not requesting that EPA adopt a final rule that differs substantially from the proposed rule or incorporate into its final rule any considerations outside of the scope of the proposed rule. The proposed rule has already provided interested parties with adequate notice and opportunity to comment, therefore there is no need to reissue another proposal.[1]

Definitions

EPA specifically requested comment on whether it should define certain terms like "best available science," "weight of the evidence," "sufficiency of information," "reasonably available information" and "unreasonable risk" in the rule itself.[2] EWG does not recommend codifying any of these definitions in the final rule or through formal rulemaking. Instead, EWG recommends that EPA address these scientific standards in guidance so as to maintain regulatory flexibility.

Scientific standards

The terms "best available science," "weight of the evidence," "sufficiency of information," and "reasonably available information" are scientific standards, largely drawn from section 26 of the new law,[3] which governs administration. Section 26 makes clear that EPA must make decisions consistent with the "best available science,"[4] "based on the weight of the scientific evidence"[5]

[1] See, e.g., International Harvester Co. v. Ruckelshaus, 478 F.2d 615, 632 n.51 (1973); South Terminal Corp. v. EPA, 504 F.2d 646, 659 (1st Cir. 1974).
[2] Procedures for Chemical Risk Evaluation Under the Amended TSCA, 82 Fed. Reg. 7562, 7572 (proposed Jan. 19, 2017) (to be codified at 40 C.F.R. pt. 702).
[3] 15 U.S.C. §§ 2625(h)-(k).
[4] 15 U.S.C. § 2625(h).
[5] 15 U.S.C. § 2625(i).

and taking into consideration information that "is reasonably available to the Administrator"[6] under sections 4, 5, and 6 of TSCA. Codifying definitions of these scientific standards does not alter their mandatory application to section 4, 5, and 6 decisions, but limits how EPA can interpret and apply them.

EWG sees no benefit to this approach. These scientific standards are addressed in EPA guidance and policy documents.[7] Codifying definitions, therefore, provides no meaningful additional regulatory certainty and instead would unduly constrain EPA. The science of risk-based chemical assessments is constantly evolving and EPA should have regulatory flexibility to adjust its analysis as new science becomes the "best available" science, without having to rewrite the risk evaluation rule.

Furthermore, codifying these science standards runs counter to the purpose of the risk evaluation rule. The Lautenberg Act requires EPA to establish a *process* for performing evaluations on chemicals.[8] In light of this requirement, in August 2016, EWG[9] and several other environmental and public health NGOs[10] specifically requested that EPA craft a rule that was *procedural* in nature.[11] At the time, EWG stated that the proposed rule should "establish a framework for risk evaluation but need not delve deeply into detail on the scientific methodologies and information requirements."[12] The final rule must provide flexibility to apply scientific standards in the way that makes most sense for a substance's particular conditions of use, specific subpopulations affected, and evolving understanding of risk. Imposing a rigid one-size-fits-all framework for science standards would undermine EPA discretion and remove this needed flexibility.

---

[6] 15 U.S.C. § 2625(k).

[7] Cf., e.g., U.S. EPA, Office of the Science Advisor, Risk Assessment Forum, EPA/100/R–14/001, Framework for Human Health Risk Assessment to Inform Decision Making (2014) (available science); EPA, Office of Policy, Economics and Innovation, Guide to Considering Children's Health When Developing EPA Actions (2006) ("best available" information, available information); EPA, Risk Assessment Forum, EPA/630/P-03/001F, Guidelines for Carcinogen Risk Assessment (2005) (weight of evidence, sufficiency of information); EPA, Science Policy Council, EPA 100-B-00-002, Risk Characterization Handbook (2000); EPA, EPA-HQ-OPPT-2010-0877-0021, Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening to Identify the Need for Tier 2 Testing (2011) (weight of evidence, sufficiency of information, available science); EPA, Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464 (proposed Jan. 19, 2017) (to be codified at 40 C.F.R. pt. 751) (best available science, reasonably available information).

[8] 15 U.S.C. § 2605(b)(4)(B) (emphasis added).

[9] Envtl. Working Grp., Comment Letter on Proposed Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0027.

[10] E.g., Earthjustice, et. al., Comment Letter on Proposed Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0067; Envtl. Def. Fund, Comment Letter on Proposed Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0026; Natural Res. Def. Council, Comment Letter on Proposed Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0024; Safer Chems., Healthy Families, et. al., Comment Letter on Proposed Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0019.

[11] Envtl. Working Grp., supra note 9.

[12] Id.

EWG continues to recommend that EPA instead address these scientific standards in guidance, which EPA is required to promulgate within two years of enactment and update every five years under Section 26(l).[13] With such frequent updates, EWG is confident that guidance can provide stakeholders with sufficient regulatory clarity without unduly burdening EPA and undermining the risk evaluation process. Although EPA is not required to solicit public comment on these guidance and policy documents, EWG encourages it to do so as the public—including industry, advocates, and academics—may have valuable insight on the most current scientific standards.

Unreasonable risk

EPA has also requested comment on whether to codify the definition of "unreasonable risk" in the proposed risk evaluation rule. EWG believes this definition should not be codified in the final rule.

The unique nature of chemical regulation under the amended TSCA makes it difficult to create a one-size-fits-all safety standard. TSCA regulations must cover all the conditions of use for a chemical substance throughout its entire lifecycle (including but not limited to manufacturing, industrial and consumer uses, recycling and disposal, and any other reasonably foreseeable uses) and account for any potentially exposed or susceptible subpopulations. Given the broad universe of uses, the safety standard therefore must be applied with flexibility and discretion on a case-by-case basis.

Codifying a rigid one-size-fits-all definition of "unreasonable risk"[14] runs the risk of unduly narrowing EPA analysis, removing needed discretion, and preventing EPA from quickly updating its unreasonable risk analysis as the science evolves.

EWG does support EPA's decision to list some of the factors it plans to consider in the preamble to the rule. EPA has indicated that it will consider "characterization of cancer and non-cancer risks (including margins of exposure for non-cancer risks), the population exposed (including any susceptible populations), the severity of hazard (the nature of the hazard), the irreversibility

[13] 15 U.S.C. §§ 2625(l)(1)-(2).

[14] While EWG does not support codifying a definition of unreasonable risk, should EPA define unreasonable risk, EWG would expect such a definition to be entirely health and environmentally based, and exclude any consideration of costs or a chemical's benefits. EWG would further expect such definition to be at least as health-protective as the "reasonable certainty of no harm" standard applied to pesticides under the Food Quality Protection Act. The definition should account for potentially exposed or susceptible populations, take into consideration aggregate and cumulative exposures, should follow National Academy of Sciences recommendations for a unified dose-response framework using a 95 percent confidence interval at a set population risk, and require unreasonable risk to be found whenever there is a cancer risk greater than or equal to one case of cancer per 1,000,000 people. Any definition should reflect that "unreasonable risk" is the possibility of harm, not the certainty of harm. *See* Nat'l Acad. Sci., Science and Decisions: Advancing Risk Assessment (2009), http://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment

of hazard, uncertainties, and estimates of cumulative exposure."[15] However, EWG cautions that these factors should be considered as starting points only, and amended slightly.

Specifically, EWG suggests changing "risk" to "hazard" when discussing "characterization of cancer and non-cancer risks," consistent with section 6(b)(4)(D).[16] EPA should remove methods from the list of factors, especially the reference to "margins of exposure," which EWG believes is inadequate for assessing non-cancer hazards. "Irreversibility of hazard" should also be removed. EPA should further consider ecological risks in addition to human health effects. Above all, as emphasized in comments submitted in August by leading science academics, EPA guidance should reflect that risk, by definition, is the *possibility* of harm, not the certainty of harm.[17]

Proposed new definitions

EPA includes new definitions in the proposed rule for "aggregate exposure," "sentinel exposure," "pathways," "routes," "uncertainties," and "variables" in the proposed rule. It also enhances the definition of "potentially exposed or susceptible subpopulations."

EWG overall supports these new definitions, while providing additional recommendations on how to improve and enhance them. In particular, EWG supports the expansion of the "potentially exposed or susceptible populations" definition by adding the phrase "including, but not limited to" before listing the subpopulations. EWG further supports the added language to "include specific authorization for EPA to consider both intrinsic (*e.g.,* life stage, reproductive status, age, gender, genetic traits) and acquired (*e.g.,* pre-existing disease, geography, socioeconomic, cultural, workplace) factors when identifying this population."[18] There is significant scientific evidence that both intrinsic and acquired factors can make individuals and populations more vulnerable to harm from toxic chemicals.[19] These enhancements and specific authorizations will help EPA conduct more thorough risk evaluations and better consider all conditions of use for a particular chemical, as required by the statute.

For the definition of "pathways of exposure" EWG recommends adding "dust" to the list of means by which people are exposed. Dust has emerged as an important pathway, especially for

[15] 82 Fed. Reg. at 7566.
[16] 15 U.S.C. § 2605(b)(4)(D).
[17] Comment Submitted by U.S. Academic Scientists on Risk Evaluation Procedural Rule under TSCA section 6(b)(4) (Aug. 24, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0400-0071.
[18] 82 Fed. Reg. at 7576.
[19] See National Academy of Sciences, Science and Decisions: Advancing Risk Assessment (2009), available at https://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment.

children. For example, dust is a key pathway of exposure for HBCD,[20] one of the first 10 chemicals selected to undergo risk evaluation under the Lautenberg Act.

As expressed in more detail below, EWG has significant concerns about sentinel exposure analysis. The proposed definition for "sentinel exposure" discusses exposure of "greatest significance" and references the "plausible maximum exposure" to an individual or population.[21] The term "greatest significance" is vague. The definition indicates that a "plausible maximum exposure" *may* be significant but does not indicate what else EPA might consider "significant."[22] Further, it assumes that a plausible maximum exposure can be measured, and does not explain if or how populations that are differently affected will be taken into account. EPA should either remove or redraft this definition and adopt a position that sentinel exposure cannot and should not displace aggregate exposure analysis.

Manufacturer-requested risk evaluations

Process & information requirements

EWG strongly supports EPA's proposed procedure for manufacturer requests. Under the statute, EPA has significant discretion to establish the form, manner, and criteria for manufacturer-requested risk evaluations.[23] EWG fully expects that any manufacturer-requested chemical will undergo the same robust risk evaluation process as prioritized chemicals. Because manufacturer-requested chemicals will not undergo a pre-prioritization information collection period, EWG supports the requirement to only accept manufacturer requests submitted with adequate information to complete a risk evaluation.[24] That must include information on all conditions of use, and potentially exposed or susceptible subpopulations. The information must already be in EPA's possession or easily obtainable (*e.g.*, an article in a scientific journal published online). If the information is in the requestor's possession but not publicly available, it must be included with the request. EWG strongly supports the proposal that EPA reject any request relying on information known to the requestor, but in the possession of another entity.[25] If EPA accepts a manufacturer request, it should publish a list of the information referenced or provided in the scoping document and accept comment on whether that information is sufficient to complete a risk assessment.

---

[20] Laurence Roosens, et. al., Exposure to HBCDs via Dust Ingestion, but Not Diet, Correlates with Concentrations in Human Serum, 117 Envtl. Health Perspectives 1707 (2009), available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2801203; cf. Cassandra Rauert, et. al, Direct contact between dust and HBCD-treated fabrics is an important source of surface-to-dust transfer, 545-46 Science of the Total Environment 77 (2016), available at http://www.sciencedirect.com/science/article/pii/S0048969715312109.

[21] 82 Fed. Reg. at 7576 (to be codified at 40 C.F.R. pt. 702.33).

[22] Id.

[23] 15 U.S.C. § 2605(b)(4)(C).

[24] 82 Fed. Reg. at 7576 (to be codified at 15 C.F.R. § 702.37(a)).

[25] Id. at 7569 ("EPA will not accept a manufacturer request where any of the relevant data is not in the possession of the requestor but is with another entity").

Unpublished information

EPA specifically requested comments regarding the use of unpublished information in manufacturer-requested risk evaluations.[26] While considering unpublished data or other proprietary documents may be informative, it is imperative that EPA assess any potential biases and limitations in the collection, analysis, or preparation of that information. This is especially important when considering unpublished information obtained from requestors with a clear interest in the outcome of any potential regulatory decision (*e.g.*, entities with a financial interest in the manufacture or use of a chemical). Determining the strength of any dataset, study, or information—and assessing bias and limitations of these sources of information—requires clear and detailed documentation of methodology on study design, sample size, analysis, and other relevant information. Further, the unpublished sources of information must include an accompanying disclosure of financial or other interests of the parties submitting such information.

EWG strongly supports expanding reporting requirements sections 8(a) and 8(d) so that EPA has a wider variety of unpublished studies in its possession, rather than having to rely on information submitted by the requestor.

Prioritizing manufacturer-requested chemical reviews

For chemicals that meet EPA's information criteria, the statute obligates EPA to review enough manufacturer-requested chemicals to make up 25 to 50 percent of all chemical substances under review.[27] In the event that EPA receives enough compliant requests to exceed this 50 percent cap, EPA has proposed giving preference to chemicals where states have imposed restrictions affecting commerce, health, or the environment (as required by statute),[28] and chemicals with likely high exposures and/or hazards under one or more conditions of use. EWG supports giving priority to chemicals that are likely to cause the greatest harm. However, because understanding of risk and hazard is constantly evolving, EWG strongly supports the proposed catch-all provision allowing manufacturer requests to be selected based on "any other factor EPA determines to be relevant."[29]

Peer review

EPA specifically requested comment on peer review. Because EPA will be relying on information collected and submitted by manufacturers, who generally will have an interest in the

[26] 82 Fed. Reg. at 7572-73.
[27] 15 U.S.C. § 2605(b)(4)(E).
[28] Id. § 2605(b)(4)(E)(iii).
[29] 82 Fed. Reg. at 7577 (proposed) (to be codified at 15 C.F.R. § 702.37(e)(5)(iii)).

outcome of the risk evaluation, it is of particular importance that the science underlying these assessments undergoes peer review. Requiring peer review for these manufacturer-requested reviews would add needed transparency and accountability to the process. However, in cases where EPA has determined that a chemical presents an unreasonable risk and risk-management action is needed to prevent additional harm to human health or the environment, the time necessary for the peer-review processes should not hinder prompt action.

Fees

The proposed rule specifies that, as required by the statute, manufacturers must pay for the costs of the risk evaluations they request.[30] However, the proposed rule fails to specify *when* manufacturers must pay these fees. To ensure EPA has the resources to complete a timely evaluation, EWG suggests the proposed rule clarify that the requestor must pay the fees *before* EPA initiates the evaluation.

Scope of risk evaluation

Observations made in previous comments to EPA regarding the appropriate scope of risk evaluations for the first 10 chemicals, submitted by Earthjustice in March of this year on behalf of numerous environmental and public interest groups including EWG, are also applicable to this proposed rule.[31] The following comments on the proposed scoping process largely echo those made by Earthjustice in March.

Identifying 'conditions of use'

As the proposed rule recognizes, "conditions of use" under the new statute are clearly defined to include not only what the manufacturer has identified as intended uses, but also any uses that can be "reasonably foreseen."[32] In the scope of the risk assessment, EPA must account for the entire lifecycle of the chemical, including risks during production, processing, distribution, recycling, and disposal. A full picture of a substance's "conditions of use" therefore includes the historical or "legacy" uses of the substance and uses not regulated under the statute.

When EPA identifies the conditions of use to be assessed during a risk evaluation, such conditions must also include accidents and misuses, even when misuses violate the law. In order to comply with the statute's requirement that the agency consider all "reasonably foreseen" conditions of use,[33] EPA must identify any potential accidental, off-label, and illegal

[30] 82 Fed. Reg. at 7577 (proposed)(to be codified at 15 C.F. R. § 702.37(f)).
[31] Alaska Community Action on Toxics, et al., Comments on Scope of the Risk Evaluations for the First Ten Chemicals under the Toxic Substances Control Act (Mar. 15, 2017).
[32] 15 U.S.C. § 2602(4).
[33] Id.

circumstances in which the substance may be manufactured, processed, distributed in commerce, used, or disposed.[34]

Furthermore, EPA should not omit a condition of use from the scope of the risk assessment because data on that particular use is lacking. Information submitted to the agency during the scoping process may not be adequate to complete the scoping documentation. EPA must actively seek "reasonably available information" about conditions of use from stakeholders in accordance with "best available science" principles.[35] The agency may need to solicit information from public health experts, government agencies, industry, communities, and consumers by, for example, reaching out to the public to determine how consumer products are actually used.[36] Additionally, EWG encourages EPA to rely on the appropriate use of defaults, or calculated uncertainty factors when specific information is missing.

Identifying hazards to 'exposed individuals and populations'

EWG encourages EPA to keep in mind that the appropriate processes and procedures to identify susceptible and highly exposed populations may be unique to each substance evaluated. For example, legacy uses of a substance may have disproportionately contaminated particular communities, or exposure to a substance may pose unique health risks for fetal or childhood development. Consequently, EWG urges the agency to seek communities and public health experts' input as to the appropriate means of identifying vulnerable and chemically overburdened populations when drafting scoping documentation. EWG also requests that EPA apply its own established principles for promoting environmental justice when determining the scope of a risk assessment.[37]

When EPA identifies "any potentially exposed or susceptible subpopulations" and "the hazards to health and the environment that EPA plans to evaluate," the agency should conduct outreach to communities likely to be home to potentially exposed or susceptible subpopulations. These communities may possess crucial information about hazards that the agency may itself lack. For example, as highlighted in the comments submitted by Earthjustice,[38] such communities are in the best position to inform EPA about nursing homes or schools located near sites that increase the likelihood of subpopulations' exposures to the chemical. Additionally, workers may be best able to identify real-world occupational exposures to chemicals, including roles and responsibilities that create highly exposed subgroups within their ranks. Other federal, state, and local regulatory authorities may also possess information necessary to establishing the proper

[34] Alaska Community Action on Toxics, et al., supra note 31.
[35] 15 U.S.C. § 2625(k), § 2605(b)(4)(F)(i).
[36] Alaska Community Action on Toxics, et al., supra note 31.
[37] EWG urges the agency to refer to the comments made by Earthjustice in March for more detail: Alaska Community Action on Toxics, et al., supra note 31.
[38] Id.

scope of a risk assessment. For example, the California EPA has developed child-specific risk values for certain chemicals, like atrazine and chlorpyrifos. Those values compare children's susceptibility to adults' by specifically examining child-specific routes of exposure.[39] EPA should review California EPA's approach and adopt its risk values as appropriate, and incorporate information from the analysis California EPA has already completed.

Proposed 'conceptual model' and 'analysis plan'

EPA proposes to include in the scoping documentation for each substance a "conceptual model" for the risk evaluation that "will consider the life cycle of the chemical substance, including manufacture, processing, distribution in commerce, storage, use, and disposal." EWG encourages EPA to ensure any conceptual models adequately consider the exposures of vulnerable and chemically overburdened populations, such as communities working and living near manufacturing, storage, use, and disposal sites.

EPA also proposes to include as part of its scoping documentation an "analysis plan" identifying the agency's strategy for the risk evaluation. As EPA develops its plan to identify approaches for addressing uncertainties, EWG urges EPA to consider real-world exposures resulting from reasonably foreseen conditions of use, such as "off label" use of consumer products or imperfect health and safety conditions in work environments. EPA should also take into consideration exposure from contaminants, such as 1,4-dioxane contamination in personal care products. The agency should make health protective assumptions that reflect exposures under realistic conditions of use.

Weight of evidence and systematic review

Section 26(i) requires EPA to make section 4, 5, and 6 decisions "based on the weight of scientific evidence."[40] In the proposed rule, EPA has declined to specifically define weight of evidence (WOE) because "this process has and will continue to evolve with changing scientific methods and innovation. Codifying a specific definition can inhibit the flexibility of the Agency to quickly adopt and implement changing science."[41] EWG supports this approach. As EPA points out, the National Academy of Sciences (NAS) has found that WOE judgments can vary significantly among experts, consensus is difficult to achieve, and evaluations are difficult to describe in anything other than general terms.[42] More recent NAS reports have criticized the term "weight of evidence" as "far too vague as used."[43] As such, WOE is difficult to apply

[39] Cal. EPA, Office of Envtl. Health Hazard Assessment, Child-Specific Reference Doses Finalized to Date, http://oehha.ca.gov/risk-assessment/chrd/table-all-chrds (Jun. 22, 2010).
[40] 15 U.S.C. § 2625(i).
[41] 82 Fed. Reg. at 7564.
[42] Id. (citing National Academy of Sciences (NAS) 2009, ref. 3.).
[43] Nat'l Acad. of Scis., Review of EPA's Integrated Risk Information System (IRIS) Process (2014).

uniformly and a formal definition would unduly restrict EPA's ability to apply WOE on a case-by-case basis.

EPA also specifically requested comment on systematic review and on EPA's position that "the proposed risk evaluation process generally reflects the use of systematic review approaches that are appropriate for the types and quantity of information used in a chemical risk evaluation."[44] EWG recommends that EPA use systematic review techniques for key endpoints. Several methods for systematic review have been developed and provide a more rigorous method of assessing in-vitro, laboratory, and human studies. Systematic reviews use quantitative techniques to assess study power and the possibility of bias. As such, they are more rigorous and defensible than historic weight of evidence approaches.

Use of systematic review is also consistent with congressional intent. Indeed, the House Energy and Commerce Committee Report on H.R. 2576 asserted:

> The term ''weight of evidence'' refers to a systematic review method that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently, identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance. This requirement is not intended to prevent the Agency from considering academic studies, or any other category of study. The Committee expects that when EPA makes a weight of the evidence decision it will fully describe its use and methods.[45]

EWG recommends that EPA's methods for systematic review of safety information align with the National Toxicology Program's Office of Health Assessment and Translation (OHAT) guidelines,[46] and the "Navigation Guide" approach developed by the University of California, San Francisco.[47] The process should be robust and transparent, and EPA should conduct an exhaustive literature review, clearly publish the inclusion/exclusion criteria and guidelines used for each problem formulation and risk assessment, screen for bias (especially financial conflicts of interest), and evaluate the quality and strength of the overall body of evidence. Failure to meet all criteria should not necessarily result in the automatic exclusion of a particular study, but it may influence how the study is weighted in an assessment. If studies are excluded from

---

[44] 82 Fed. Reg. at 7564.
[45] H.R. Rep. No.114-176, at 33 (2015), https://www.congress.gov/114/crpt/hrpt176/CRPT-114hrpt176.pdf (emphasis added).
[46] Nat'l Toxicology Program, OHAT Systematic Review, https://ntp.niehs.nih.gov/pubhealth/hat/noms/index-2.html (last visited March 20, 2017).
[47] Tracey J. Woodruff, Patrice Sutton, & The Navigation Guide Work Grp., An Evidence-Based Medicine Methodology to Bridge the Gap Between Clinical & Envtl. Health Sci., 35 Health Affairs 931 (2011), http://content.healthaffairs.org/content/30/5/931.full.pdf+html?ijkey=z58MCEPW2X49.&keytype=ref&siteid=healthaff.

consideration, the rationale should be transparent to the public. Scholars have pointed out that good laboratory practices (GLP) are often not associated with higher quality research, proper study design, or correct statistical analysis.[48] Thus, studies that do not meet GLP standards or test guidelines, such as OECD, should not be excluded automatically.

Aggregate, cumulative, and sentinel exposures

As part of a risk assessment, EPA is required to describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered.[49] EWG strongly believes that considering the *aggregate* exposures will provide a more robust analysis of the total risk a chemical poses. To properly assess aggregate exposures, EPA must consider exposures throughout the lifecycle of the chemical from all routes and pathways, including exposures from conditions of use not regulated by TSCA. For example, this would include exposures from things like food, drinking water, pesticides, and personal care products, even if those uses are not specifically regulated during section 6(a) rulemaking. EWG emphasizes that this approach should include aggregate exposures from trace contaminants, such as asbestos fibers sometimes found in talc products,[50] or 1,4-dioxane in cleaning and personal care products that contain ethoxylated ingredients.[51]

Although the statute requires EPA to describe whether it considered aggregate or sentinel exposures, there is no express requirement to conduct a sentinel exposure analysis for any particular chemical. EWG finds sentinel exposure analysis problematic and suggests that such an approach be used sparingly, if at all. According to EPA's proposed definition, sentinel exposure focuses on exposures "of the greatest significance, which may be the maximum exposure" to an individual population or the environment.[52] EWG considers such an approach inconsistent with the latest scientific research.

As EWG finds, a sentinel approach operates under an improper assumption that reducing exposure in highly exposed populations would result in reductions in risk to less-exposed populations. That is an unacceptable shortcut for evaluating real world exposures. It incorrectly assumes that risk assessors will always be able to determine the most highly exposed group. It fails to account for how different, and potentially susceptible populations, may be differently

[48] J.P. Myers et al., Why public health agencies cannot depend on good laboratory practices as a criterion for selecting data: the case of bisphenol A, 117 Envtl. Health Perspectives 309-15 (2009), https://www.ncbi.nlm.nih.gov/pubmed/19337501.
[49] 15 U.S.C. § 2605(b)(4)(F)(ii).
[50] Ronald Gordon, et. al., Asbestos in Commercial Cosmetic Talcum Powder as a Cause of Mesothelioma in Women, 20 Int'l J. of Occupational and Envt'l Health 318 (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164883.
[51] Agency for Toxic Substances & Disease Registry, Public Health Statement for 1,4-Dioxane, Toxic Substances Portal (April 2012), https://www.atsdr.cdc.gov/phs/phs.asp?id=953&tid=199.
[52] 82 Fed. Reg. at 7576.

exposed to a chemical substance. As EWG pointed out in August 2016 comments, it also disregards the significant body of evidence that hormone disruptors and developmental toxicants may cause adverse effects at very low doses, and ignores the possibility of nonmonotonic dose-response curves.[53] The pharmaceutical literature is rife with examples of nonmonotonicity, timing, and age-group specific toxicity concerns.[54]

Although cumulative exposures are not required to be part of a risk assessment under the law, EPA has explicit authority to order testing and prescribe protocols and methodologies for a number of health and environmental effects, including "cumulative or synergistic effects."[55] People and vulnerable subpopulations can be exposed to multiple chemicals and stressors that contribute to the same adverse health effects. For example, NAS has noted the need to evaluate the cumulative effects of phthalates and also pointed to the fact that lead and mercury can collectively affect brain development.[56] Taking such cumulative impacts into consideration would improve current assessments.

Thus, cumulative exposure assessments should be done whenever possible. EPA may consider collective exposure to groups of similar chemicals, and use the Adverse Outcome Pathway framework and database[57] to identify where cumulative effects may be an issue. EPA should follow the cumulative risk assessment process recommended by NAS in its Phthalates and Cumulative Risk Report.[58] When specific information is not available, EPA may use default values to account for cumulative exposures.

Population-based risk estimates for non-cancer endpoints

EPA specifically requested comment on Margin of Exposure (MOE) assessments, which the Agency has used historically to characterize risks under TSCA.[59] EWG cautions against this approach for assessing non-cancer hazards and recommends abandoning it. The MOE approach gives no population-based risk estimation, no estimate of risks at various exposure levels, and simply serves as a cut point. MOE presumes that there is a safe level of exposure, below which no harm will occur. NAS has recommended moving away from this kind of bright line approach because it is not a valid scientific assumption for all chemicals.[60] Indeed, careful study of the

---

[53] Envtl. Working Grp., supra note 9.
[54] See, e.g., Non-monotonic Dose Response Curves, Our Stolen Future, http://www.ourstolenfuture.org/NewScience/lowdose/nonmonotonic.htm (last visited Mar. 20, 2017).
[55] 15 U.S.C. § 2603(b)(2)(A).
[56] Nat'l Acad. Sci., Phthalates and Cumulative Risk Assessment: The Tasks Ahead (2008), https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=202508.
[57] Adverse Outcome Pathway Knowledge Database, Org. for Econ. Co-Operation & Dev., http://aopkb.org/ (last visited March 20, 2016).
[58] Nat'l Acad. Sci., supra note 56.
[59] 82 Fed. Reg. at 7572.
[60] Nat'l Acad. Sci., Science and Decisions: Advancing Risk Assessment (2009), http://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment.

non-cancer toxicities of chemicals like mercury, lead, and arsenic increasingly reject the concept of a toxicological threshold, below which there is no chance of harm.

Instead, EPA should incorporate NAS's recommendations for population-based risk estimates in their risk assessments as standard practice, as described in Science and Decisions: Advancing Risk Assessment.[61] In this approach, MOE and reference doses are abandoned for a continuous dose-response approach that defaults to a linear model with no assumption that a safe exposure level exists. This change will improve assessments by providing an actual estimation of risk. EPA should further assume chemicals follow a probability of adverse effects at low levels of exposure and use tools which provide more robust assessment of data from studies of non-cancer effects.[62] Probabilistic modeling would allow EPA to better identify exposure distributions and make risk management decisions for potentially exposed and susceptible populations.

Fit for purpose

In the preamble to the risk evaluation rule, EPA proposes that the components of the risk evaluation will be "fit for purpose"[63] and that it expects to be able to reach conclusions on some conditions of use "without extensive or quantitative evaluations of risk."[64] EPA uses lower-volume and less dispersive uses as specific examples. EWG has already expressed concern about equating low volume or low exposure to low risk, especially for chemicals like endocrine-disrupting chemicals and nanomaterials known to cause harm at low doses. EWG is concerned that "fit for purpose" is too vague a term. EWG urges EPA to be transparent about its assumptions and any reasons it excludes any uses or studies from its analysis, instead of relying on vague "fit for purpose" language.

Draft risk assessments

As noted in the preamble to the rule, the Lautenberg Act requires EPA to develop guidance to assist "interested persons" in submitting draft risk evaluations for EPA consideration.[65] Although such guidance falls outside the scope of this rule, EWG believes it is important to emphasize that any draft risk evaluations prepared by third parties must, at minimum, meet all the same criteria as EPA's risk evaluations. EPA should solicit stakeholder feedback and public comment on any proposed guidance before it is finalized. Any draft risk assessments submitted by interested persons should undergo peer review before EPA can accept them. EPA must also solicit public comment on any draft risk assessments submitted by interested persons.

---

[61] Id.
[62] Salomon Sand et al., The Current State of Knowledge on the Use of the Benchmark Dose Concept in Risk Assessment, 28 J. Applied Toxicology 405 (2007), http://onlinelibrary.wiley.com/doi/10.1002/jat.1298/full.
[63] 82 Fed. Reg. at 7566.
[64] Id.
[65] Id. at 7567; 15 U.S.C. § 2625(l)(5).

Finally, in the preamble to the risk evaluation rule, in its summary of stakeholder feedback, EPA erroneously states that "due to changes in the law, *manufacturers* are now able to submit their own draft risk evaluations."[66] This characterization of the change in the law is too narrow. The statute allows for draft risk evaluations from any *interested person* which could include public health advocates or state governments. EPA should change the "manufacturer" in this sentence to "interested person" to reflect the statutory language.

Transparency

EPA also specifically requested comment on ways to increase transparency in the risk evaluation rule.[67] EWG supports the additional comment periods on the scope of proposed risk evaluations and also on manufacturer evaluations. EPA should also solicit public comment on key guidance documents, such as the guidance on draft risk assessments by interested persons.

EWG also notes that systematic review is designed to increase transparency in the risk evaluation process. As previously discussed in these comments, reliance on systematic review best practices will increase transparency in the risk evaluation process.

Conclusion

EWG appreciates the opportunity to weigh in on this proposed rule, which will play a pivotal role in the implementation of the new chemical law. EWG generally endorses the approach proposed by the EPA. EWG's comments should in no way be construed to suggest changes significant enough to trigger a reissue of the proposal rule. EWG looks forward to continuing to participate in the TSCA implementation process. Any questions on these comments or other aspects of TSCA implementation should be directed to Melanie Benesh, Legislative Attorney, mbenesh@ewg.org, 202-939-0120.

[66] Fed. Reg., supra note 2, at 7567.
[67] Id. at 7565.